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ORIGINAL ARTICLE

Epidemiological, diagnostic, and therapeutic aspects of community-acquired complicated intra-abdominal infections at the university hospital center of Constantine, Algeria

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ABSTRACT

Introduction and objectives: Intra-abdominal infections are the leading non-traumatic surgical emergencies, with persistently high morbidity and mortality. The objective of our work is to report the epidemiological, clinical, diagnostic, and therapeutic aspects of complicated community-acquired intra-abdominal infections in adults. **Patients and methods:** A prospective, descriptive study was conducted from September 2016 to March 2018 on a cohort of adult patients who underwent surgery for community-acquired complicated intra-abdominal infections. Data were collected using survey forms. Epidemiological, clinical, biological, radiological, therapeutic, and evolutionary variables were described. **Results:** 227 patients were recruited. Mean age was 44 ± 20 years [range: 15 to 90 years]. The sex ratio was 1.9. Twenty-six percent of patients had at least one comorbidity. The most frequent symptoms were abdominal pain (99%), signs of peritoneal irritation (89%), clinical presentation of acute appendicitis (56%), nausea and/or vomiting (46%), and occlusive syndrome (22%). Fever was present in 45% of patients; 7% had signs of severity at admission. The source of contamination was appendicular in more than 50% of cases. Empirical antibiotic therapy consisted of cefazolin in 75% of cases; 49% received triple therapy with gentamicin and metronidazole, and 25% received dual therapy with metronidazole. Cefotaxime was prescribed in severe cases or in the presence of comorbidities. Peritoneal fluid culture was positive in 58% of cases, with *Escherichia coli* isolated in 51%. The mortality rate was 15.4%. **Discussion and conclusion:** Intra-abdominal infections were of appendicular origin in more than half of the cases in our series. Mortality was associated with advanced age, presence of comorbidities, severity of the initial clinical presentation, and colorectal origin of the infection.

Keywords: intra-abdominal infections, epidemiology, diagnosis, empirical antibiotic therapy, microbiology.

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1. INTRODUCTION

Intra-abdominal infections (IAIs) represent the main non-traumatic surgical emergencies. They are the second leading cause of septic shock after pulmonary infections [1] and the leading non-traumatic cause of death in emergency surgery departments [2]. They are characterized by the extreme heterogeneity of their clinical presentations. IAIs are said to be simple when the infectious process remains limited to a single organ and does not extend to the peritoneum. This is the case with simple, uncomplicated acute

appendicitis or uncomplicated acute cholecystitis. These infections can be treated by surgical resection or antibiotic therapy. IAIs are said to be complicated when the infectious process extends beyond the affected organ and causes localized or generalized peritonitis, Patients urgently need surgical control of the infectious source and antibiotic therapy [2, 4-6]. The management of IAIs must always be early and multidisciplinary, the main objective being to identify severe and high-risk patients in order to quickly initiate effective resuscitation and prepare the patient for the surgical procedure, which remains the cornerstone of treatment [5]. Antibiotic treatment (ATB) has shown its effectiveness in terms of perioperative morbidity and mortality [7-9]. It must be started as soon as the diagnosis is established, especially in cases of severe signs and septic shock [3-5, 10]. It must target the most frequently involved microorganisms, namely enterobacteria and anaerobes, based on local ecological data [2-5, 11-16]. The objective of this article is to provide a synthesis of the etiological, clinical, radiological, biological, and therapeutic aspects of complicated community-acquired IAIs in adults through the experience of the surgical emergency department (SED) of the Constantine University Hospital Center.

2. PATIENTS AND METHODS

This is a prospective, descriptive, observational, monocentric study in the surgical emergency department of the Benbadis University Hospital Center (UHC) of Constantine, over a period of 19 months, from September 1, 2016, to March 31, 2018, conducted on all patients over 15 years old operated on for complicated community-acquired IAI with perioperative peritoneal fluid (PF) sampling. The diagnosis of complicated community-acquired IAI (cIAI) was made in the presence of an acute abdominal syndrome, onset in the city or during hospitalization of less than 48 hours, imaging suggestive of IAI, hyperleukocytosis with neutrophil polymorphonuclear leukocytes (PMNs) greater than 10,000/mm³ (C-reactive protein (CRP) measurement was not available), and indication for surgical treatment. Severe forms of IAI were defined by the presence of clinical manifestations related to sepsis or septic shock. Postoperative peritonitis, primary peritonitis, and focal infections such as biliary infections and isolated liver abscesses were excluded from our study. The peritoneal sampling was performed as soon as the peritoneum was opened before any surgical maneuvers in sterile syringes. All samples were analyzed at the microbiology department of the Constantine University Hospital. Only the search for aerobic bacteria was carried out. For the preparation of our work, we relied on the data contained in medical observations and the surgical report register. These data were processed using forms including routine data (epidemiological, clinical, biological, radiological, and therapeutic). The data from the survey forms were entered into the Epi-Info Version 3.5.1 software and analyzed using the SPSS software.

Ethical statement

This study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Verbal informed consent was obtained from all included patients after providing complete information about the study's objectives, with their right to withdraw at any time respected. Written consent was not required for the observational nature of the study and local ethical guidelines. Anonymity and data confidentiality were strictly maintained. Formal authorization was obtained from the local administration of CHU Benbadis.

3. RESULTS

During the study period, 227 patients operated on for complicated community-acquired IAIs were recruited.

Description of the population: The average age of the patients was 44±20 years, with a standard deviation of 19.6 and extremes ranging from 15 to 90 years. The age group between 20 and 29 years was the most affected (21%). The sex ratio was 1.9 (66% men / 34% women). 8% of the patients had at least two comorbidities. These were mainly cardiovascular diseases (15%), diabetes (11%), and gastroduodenal ulcers (4%). Cancers were rare (2%).

Clinical presentation: Abdominal pain and signs of peritoneal irritation were present in the majority of patients with respective rates of 99% and 89%. The presence of a clear appendicular syndrome at admission was noted in 56% of the patients. Nausea and/or vomiting were less frequent (46%). An occlusive syndrome was observed in 22% of patients, while constipation was reported in only 9% of cases. Traumatic abdominal wounds were rare (2%) (Table 1). For general signs, fever was present in 45% of patients. The signs of severity were present at admission in varying proportions. The average blood pressure below 65 mmHg (7%), polypnea (18%). ASA greater than II (6%). (ASA: American Society of Anesthesiologists physical status scale)

Biological and imaging data: Hyperleukocytosis with PMNs was present in 79% of cases. The blood creatinine level was higher than 20 mg/l in 16 patients (9%). The presence of pneumoperitoneum was found in 26% of cases. Table II summarizes the radiological examinations performed during the study.

Table 1. Frequency of digestive signs.

Clinical Sign	Number	%*	Not specified(n)
Abdominal pain	222	98.6	2
Signs of peritoneal irritation (guarding/rigidity)	203	89.4	0
Appendicular syndrome	110	56.4	32
Nausea and/or vomiting	104	45.8	0
Occlusive syndrome	49	22.1	5
Constipation	21	9.3	0
Penetrating abdominal wound	4	1.8	0

Table 2. Radiological examinations performed (n=223).

Radiological examinations	%
ASP	8.5%
ASP+ ultrasound	35.4%
ASP+ ultrasound+CT scan	16%
ASP+CT	13.4%
Echography	13.4%
Echography +CT	5.9%
CT scan	7%
Not reported	1.8%

Microbiological data: The culture was positive in 58% of the cases. The PF samples were monomicrobial in 93 patients (71%), with two germs in 36 patients (27%) and with three germs in two patients (2%). In total, 171 microorganisms were isolated in the peritoneal fluid, including 160 bacterial strains and 11 yeasts. The main microorganisms isolated from our patients were primarily enterobacteria, with *Escherichia coli* leading the way, followed by *Klebsiella spp*., Enterobacter spp.

Among the non-fermenting Gram-negative bacteria, *Pseudomonas aeruginosa* was isolated in 10 patients. Gram-positive cocci, notably *Enterococcus faecalis* and *Enterococcus faecium*, were rarely isolated in our patients (table 3).

Table 3. Isolated bacterial strains (n=160).

Microorganism	Number	% (among all isolated bacteria)
Gram-negative bacilli	138	86
Escherichia coli	81	50.6
Klebsiella spp.	23	14.4
Enterobacter spp.	10	6.3
Proteus mirabilis	4	2.5
Pseudomonas Aeruginosa	10	6.3
Morganella morganii	3	1.9
Enterobacter cloacae	1	0.6
Hafnia alvei	1	0.6
Citrobacter spp.	1	0.6
Proteus vulgaris	1	0.6
Salmonella enteritidis	1	0.6
Serratia liquefaciens	1	0.6
NFGNB	1	0.6
Gram-positive cocci	22	14
Streptococcus viridans α hemo	7	4.4
Enterococcus faecalis	5	3.1
Enterococcus faecium	2	1.3
Streptococcus spp.	5	3.1
Streptococcus oralis	2	1.3
Staphylococcus aureus	1	0.6
Total	160	100

Among the isolated *Escherichia coli* strains, 75.3% were resistant (R+I) to amoxicillin, more than 75% to piperacillin and ticarcillin, 57% to amoxicillin-clavulanic acid, 37% to cefazolin, 11% to cefotaxime, 10% to gentamicin, 30% to ciprofloxacin, and 56% to cotrimoxazole. No carbapenemase-secreting strains were isolated (table 4).

Table 4. Sensitivity of Escherichia coli (n=81).

Name of the antibiotic	n (tested strains)	% R	% I	% S
Amoxicillin	81	74.1	1.2	24.7
Amoxicillin/Clavulanic acid	76	53.9	2.6	43.4
Ticarcillin	81	75.3	0	24.7
Piperacillin	66	75.8	1.5	22.7
Cefazolin	79	31.6	5.1	63.3
Cefoxitin	81	2.5	0	97.5
Cefotaxime	81	11.1	0	88.9
Aztreonam	27	18.5	0	81,5
Imipenem	81	0	0	100
Gentamicin	79	10.1	0	89.9
Amikacin	26	0	0	100
Nalidixic acid	80	35	0	65
Ciprofloxacin	77	24.7	5.2	70.1
Cotrimoxazole	79	55.7	0	44.3
Fosfomycin	65	0	0	100
Colistin	79	0	0	100
Chloramphenicol	37	5.4	0	94.6

Therapeutic aspects: The time between the surgical intervention and the diagnosis was less than 24 hours in 90% of the cases. The infection of appendiceal origin was the most frequent, accounting for 52% of cases.

Empirical antibiotic therapy: Several combinations of antibiotics were prescribed for our patients. The most frequent combination was cefazolin/gentamicin/metronidazole in 49% of cases, followed by the combination cefazolin/metronidazole in 25% of cases. The third-generation cephalosporin used was cefotaxime, which was prescribed in severe cases in combination with gentamicin and metronidazole (16%). The antibiotic treatment was appropriate in 77% of patients and inappropriate in 23% of patients. The average duration of antibiotic therapy was 10 days ± 2 days [7 - 20 days].

Evolutionary aspects: The outcome was favorable in 84% of the patients. A relaparotomy was performed in 2 patients for postoperative peritonitis. 9% of the patients had developed a postoperative nosocomial infection. The mortality rate was 15.4%.

The average length of hospital stay was 6.5 days with a standard deviation of 4.4 days [1-34 days]. More than 50% of the patients stayed less than 7 days in the hospital. The bivariate analysis of factors associated with mortality had shown that age, the presence of signs of severity, the colorectal origin of the infection, a prolonged hospital stay, and polymicrobial samples were risk factors for mortality (table 5).

4. DISCUSSION

General characteristics: The average age of our patients is lower than that found in international [14, 16, 17] and European [12, 18, 19] studies and close to that found in Moroccan, Asian, and African studies [20-22]. In developed countries, IAIs mainly affect individuals over 50 years old, which is related to the aging of the population in these countries [12, 16, 18, 19, 23]. On the contrary, in developing countries, the average age is below 50 years [13, 20, 22-25]. This would be related to the demographic and socioeconomic characteristics in these regions. The predominance of the male sex is classic in IAI; it has been found in the majority of studies, and it is particularly pronounced in developing countries [13, 20, 22, 24, 25].

Comorbidities: Our results are comparable to those found in French series [12, 18]. On the contrary, in Colombian and Serbian series, the percentages of patients with at least one comorbidity were very high [13, 23]. The nature of the underlying conditions was different; for example, in the study conducted by Montravers, neoplasms were present in 12% of the patients, as were cardiac conditions, and only 8% of their patients had diabetes [12]. These comorbidities are almost absent in African studies due to the young age of their patients [22, 24].

Table 5. Bivariate analysis of factors associated with mortality

Parameters	Survivors	Deceased	*P* value
Age ≥ 70 years	14	13	
Average age (years)	41	60	< 0.001
Gender:			
Men	125	24	0.9
Women	66	12	
Comorbidities	57	19	0.003
Intervention time> 24H	18	5	0.6
Location of the infection			
Appendicular	112	4	
Colorectal	17	4	< 0.001
Small intestine	18	11	
Gastroduodenal	38	14	0.004
Biliary	3	3	
Previous antibiotic therapy	22	3	0.02
Fever	93	8	0.003
Hyperleukocytosis	115	12	0.005
Leukopenia	2	4	
MAP < 65 mmhg	1	12	< 0.001
PAS < 90 mmhg	2	14	< 0.001
Respiratory rate (RR) > 24	22	14	< 0.001
breaths/min	4	6	0,004
HR > 120 bpm	5	11	< 0.001
Creatinine >20mg/l	6	8	< 0.001
ASA (III and IV)			
Culture PF +	106	26	0,06
2 germs	30	6	0.03
3 germs	0	2	
Enterococcus	6	1	0.1
Escherichia coli	59	13	0.2
Pseudomonas aeruginosa	8	1	0.1
Yeasts	3	0	0.5
Length of stay (average in days)	3	7	< 0.001
Appropriate antibiotic therapy	69	19	0.09

Clinical characteristics: Abdominal pain and signs of peritoneal irritation are among the classic signs of IAI [2, 3, 26]. Our figures are comparable to those found in other studies [14, 16, 21-25, 27]. Nausea and/or vomiting, although they are classic signs of foodborne illnesses, were less frequent in our study and were present in 46% of our patients. This figure is comparable to that found in several series in countries with limited or overpopulated resources [21, 22, 24, 27]. The presence of an occlusive syndrome was often linked to colonic pathology in our series; it was present in 22% of cases. These data are compatible with the results of literature series [23, 25, 27].

General signs: Fever is often cited in IAI without it being a constant sign [2-4]. It was present in 45% of patients. Signs of severity should be systematically sought in IAI, both clinically and biologically. Their presence is strongly associated with an increased risk of complications and mortality [2-5, 18, 28, 29].

Source of infection: The appendiceal origin is the most frequent in most studies. In developed countries, the colonic origin of IAI is common, but gastroduodenal perforations are rarer due to better management of gastroduodenal ulcers [12, 19, 30-32]. On the contrary, ulcer-related perforations are still very common in Africa and some Asian countries [20-22, 24, 25, 27, 33]. Typhoid intestinal perforations are a real public health problem in some African countries and in Southeast Asia, especially in the pediatric population [21, 22, 24, 25, 34]. Post-traumatic peritonitis is mainly seen in countries with war conflicts or high crime rates, such as Chad, where post-traumatic peritonitis from stab wounds is the leading cause of IAIs in the country [24].

Additional examinations: Radiological examinations are variably prescribed in different international studies depending on the patient's condition at admission, the presence or absence of signs of severity, and the availability of imaging in each country.

The scanner is not always available in emergency facilities in countries with limited resources [22]. Our data is comparable to that found in European and international studies (Table VI). The indication for medical imaging examinations must follow a logical approach, taking into account the results of the clinical and laboratory examination. In a stable patient whose surgical indication can be deferred, the CT scan is the most effective radiological examination for the diagnosis of an IAI [4]. In practice, for the diagnosis of appendicitis and diverticulitis, some authors propose performing an ultrasound first. In case of an inconclusive ultrasound examination, a CT scan is indicated [2]. Imaging tests are not necessary for patients who show obvious signs of generalized peritonitis and need to be operated on urgently [4].

Table 6. Frequency of imaging examinations prescribed in our series and in international series.

Radiological examinations	IAO study* Europe (2152 patients, 79% of whom are community-acquired)	CIAOW** study World (1898 patients, 86.7% of whom are community-acquired)	Our study (227 patients)
ASP	9.2%	12.6%	8.5%
ASP+ ultrasound	18.6%	18.7%	35.4%
ASP+ ultrasound+CT	9.5%	5.9%	16%
ASP+TDM	7.6%	5.4%	13.4%
Echography	16%	20.2%	13.4%
Echography +TDM	8.3%	4.6%	5.9%
TDM	24.5%	22.4%	7%
ASP+Echography +MRI	0.1%	0.2%	-
Ultrasound+TDM+MRI	0.2%	0.05%	-
ASP+Echography +TDM+MRI	-	0.4%	-
Echography +MRI	0.3%	0.1%	-
TDM+MRI	-	0.1%	
MRI	-	0.05%	
Not reported	6%	9.1%	1.8%

*CIAO Europe, complicated intra-abdominal infections observational study in Europe (20 European countries) [16] **CIAOW, complicated intraabdominal infections worldwide observational study [14].

Microbiological aspects: The indication of peroperative samples has been debated in recent years during international consensus conferences on IAIs. These samples are optional in cases of community-acquired IAIs without signs of severity. However, in light of the emergence of resistant bacteria in the community, particularly extended-spectrum beta-lactamase (ESBL)-producing enterobacteria, the majority of learned societies recommend their performance when possible, for monitoring the evolution of local bacterial resistance [2-6, 10, 28]. The PF culture was positive in 58% of the cases. This figure is consistent with the data from the literature [14, 16, 20].

Germs responsible for IAIs: Our microbiological data is consistent with the classical data on the microbiology of IAIs in the literature [12, 14, 16, 18, 35-37]. The rate of Gram-positive cocci isolated was nevertheless higher in the European series [12, 16]. The therapeutic impact of these results is very important because they support the recommendations of learned societies regarding probabilistic antibiotic treatment in community-acquired IAIs, which should always target enterobacteria and anaerobes.

Sensitivity to ATB: The main messages to take away from the sensitivity study of Escherichia coli strains responsible for community-acquired IAIs in our study are the loss of effectiveness of cefazolin, the combination of amoxicillin/clavulanic acid, cotrimoxazole, and ciprofloxacin against enterobacteria, with a rate of 7% ESBL among all isolated enterobacteria.

Therapeutic and evolutionary characteristics: Controlling the source of the infection is a crucial step in the treatment of IAIs and is key to therapeutic success [26, 38, 39]. The time between diagnosis and surgical intervention was less than 24 hours in the majority of cases in our study. It has been well demonstrated that early control of the source of infection is associated with good disease progression [2-5, 38, 40-44]. In our study, bivariate analysis did not find a statistically significant relationship between surgery delay exceeding 24 hours and an increased risk of mortality. This would be related to the small number of patients operated on beyond 24 hours (10% of patients).

Laparotomy under general anesthesia was performed on all patients in this series. Interventional radiology for percutaneous drainage and laparoscopic means are not available at the surgical emergency department of the Benbadis University Hospital Center (UHC). The indications for percutaneous drainage are limited in community-acquired IAIs: single collection, complicated diverticular

sigmoiditis, or appendiceal abscess, but never in cases of generalized peritonitis. Severe forms must be operated on urgently [2-4, 6, 45-48].

Empirical antibiotic therapy: The data regarding antibiotic therapy was not available for all patients; the absence of an empirical antibiotic therapy protocol in the surgical emergency department explains the heterogeneous nature of the prescriptions and duration. Therapeutic protocols in the form of written documents are strongly recommended [2-6]. In all cases, empirical treatment must target enterobacteria and anaerobes. The choice of the molecule is mainly guided by the epidemiology of the sensitivity of the most frequently isolated microorganisms. In our study, the addition of the aminoglycoside to cefazolin in 49% of patients allowed for the recovery of activity against cefazolin-resistant enterobacteria. First-generation cephalosporins are no longer recommended by international scholarly societies. In French series, amoxicillin-clavulanic acid combined with gentamicin remains the frequently prescribed treatment for moderate community-acquired pneumonia (CAP), followed by the combination of a third-generation cephalosporin with metronidazole. Inappropriate antibiotic therapy has been observed and studied in several works; its frequency varies according to the series; it is 44% in France [18] and up to 78% in India [21]. In our series, it was 23%. The bivariate analysis did not show a statistically significant association between mortality and inappropriate antibiotic therapy. These results are not compatible with the results of other series. Several studies have shown that when the initial probabilistic treatment does not take into account all microorganisms, an increase in morbidity, the frequency of surgical re-interventions, and wall abscesses, as well as a prolongation of hospital stays, has been observed. Moreover, an increase in mortality is observed in patients whose antibiotic treatment is not adjusted based on the microbiological results of peritoneal samples [18, 19, 31]. Other studies have not found this correlation between morbidity and mortality and inappropriate initial antibiotic therapy [8, 12, 21, 49].

The average duration of antibiotic therapy in our series is relatively long compared to international recommendations. It was 10 days in 87% of cases, regardless of the severity and site of the infection. The misuse of antibiotics and the absence of a probabilistic antibiotic therapy protocol based on local ecology in surgical emergencies explain the relatively long treatment duration in our series. All learned societies recommend short-term treatments for community-acquired IAIs. Thus, this duration should not exceed 24 hours in cases of acute or gangrenous non-perforated appendicitis, acute or gangrenous non-perforated cholecystitis, traumatic intestinal perforation operated on within 12 hours, and gastroduodenal perforation operated on within 24 hours. A duration of 4 days or 3-5 days is sufficient in peritonitis with effective control of the source of infection [2, 3]. In patients whose source of infection has not been completely eliminated, antibiotic therapy of 5 to 7 days is the maximum duration.

Apyrexia, the resumption of intestinal transit, and the decrease in hyperleukocytosis are elements that allow for the decision to stop treatment. The lack of clinical or biological response beyond the seventh day should prompt a discussion about surgical reintervention or resistance of the responsible microorganisms [2-6, 45, 46, 48].

Average length of stay: In the international WISS study (WSES cIAIs Score Study) (WSES: World Society of Emergency Surgery), the average length of stay was 7 days [17]. The relatively short hospital stay in our series would be related to a higher number of moderately severe infections.

Mortality: The rate found in our study is comparable to that found in Colombia, India, Cameroon, and Pakistan [13, 21, 22, 25]. However, it should be noted that the study populations of these series were cohorts of generalized peritonitis with the exclusion of localized forms. In international cohorts, generally comprising more than 80% of community-acquired forms, the mortality rate ranges between 7.6% and 10.5%, which is lower than the rate found in our study [14, 16, 17].

The bivariate analysis of factors associated with mortality in our study showed that age, the presence of comorbidities, the severity of the initial clinical presentation, the colorectal origin of the infection, and polymicrobial cultures were the main factors associated with mortality. Our results are consistent with the literature data [8, 17, 18, 31].

Limitations of the study:

This study has several limitations. It is retrospective and monocentric, which may restrict the generalizability of the results. The minimum inhibitory concentrations (MICs) of the isolated Enterobacteriaceae were not available, limiting in-depth analysis of antibiotic resistance patterns. Anaerobic bacteria were not investigated, potentially underestimating the microbial spectrum, especially in intra-abdominal infections. Additionally, there was no established therapeutic protocol for empirical antibiotic therapy in intra-abdominal infections during the study period, which may have affected treatment consistency and outcomes.

5. CONCLUSION

This work was conducted to improve the management of complicated community-acquired IAIs in adults at the ICUs of the Constantine University Hospital through the study of the clinical aspects of these infections and the knowledge of the responsible microorganisms.

In our series, the frequency of severe forms with septic shock at admission was 7%. The outcome was fatal in all cases and explains the observed mortality rate. A better understanding of the management of these infections is more than necessary. The rate of ESBL-producing *Escherichia coli* was 11% among enterobacteria. The constant increase in bacterial resistance in Algeria and around the world should prompt us to strengthen the monitoring of the evolution of this resistance and to reduce the antibiotic pressure responsible for the emergence of resistant bacteria, notably through the implementation of antibiotic therapy protocols adapted to the local ecology.

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